Allowing for Variations in Multivitamin Supplement Composition Improves Nutrient Intake Estimates for Epidemiologic Studies[1]

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ABSTRACT Collecting detailed data on dietary supplement use is time-consuming for study participants and investigators, and this is particularly difficult for multivitamin use because of the many different formulations available. Therefore, many studies simply ask about the frequency of multivitamin use and assign default nutrient composition values to obtain nutrient intakes. Multivitamin supplements are important contributors to total nutrient intakes, but it is not known how default values affect the accuracy of intake estimation. In this study, nutrient intakes were calculated from multivitamins consumed by 26,735 multivitamin users who provided detailed information like product name(s) and frequency of use on a mailed questionnaire. We then recalculated the intakes, using 2 different assumptions about the composition of the multivitamin supplements: *1*) a single default composition for all products; and *2*) four default compositions, 1 for each subtype of multivitamin, i.e., one-a-day with minerals, one-a-day without minerals, B-complex or stress multivitamins, and antioxidant combinations. A total of 1246 different brands of multivitamins were reported and nutrient composition varied widely. Spearman correlation coefficient analyses, using the 4 default nutrient profiles compared with actual nutrient intakes, were >0.5 ($P < 0.001$) for 12 of 15 nutrients examined. However, correlations using the single default were lower, with only 5 correlations >0.5. Our findings suggest that a questionnaire designed to assess the composition profiles for 4 types of multivitamin products substantially improves the accuracy of nutrient-intake estimates over one that uses a single default nutrient profile for all multivitamin products. J. Nutr. 136: 1359–1364, 2006.

KEY WORDS: • *multivitamin supplements* • *nutrient intakes* • *supplement composition*

Results from national surveys confirm that a high proportion of the general U.S. population uses dietary supplements. In the National Health and Nutrition Examination Survey 1999–2000 (NHANES), 52% of adults reported taking a dietary supplement in the past month and 35% took a multivitamin with or without minerals (1). Based on data from previous NHANES surveys, dietary supplement use has increased steadily over time (1,2). There has been a dramatic increase in the dietary supplement market, which was valued at $11.8 billion in 1997, and rose to $20.3 billion in 2005 (1,3,4). Daily intake of vitamin supplements may lower the risk of chronic diseases, although results from epidemiological studies and clinical trials are inconclusive (5–14).

Because of the high prevalence of dietary supplement use, and the possibly high amount per dose for 1 or more nutrients, intakes from supplements should be assessed, as well as intakes from foods in any study that requires nutrient intake data. Not including dietary supplement use may cause a considerable misclassification of individuals with regard to total intake and rankings of intake (15,16). Studies that have compared or validated survey instruments for assessing intake from supplements alone, or from foods plus supplements, have noted the importance of using valid methods (16–21).

Reporting detailed information on all supplements that are consumed can be time-consuming for study participants, and maintaining an accurate database of the nutrient composition for each supplement can be prohibitively expensive for investigators. Therefore, particularly in large studies, questionnaires are often used that question the frequency of supplement intake using broad categories, such as "multivitamins" (22–28). A default nutrient profile is then determined for each supplement category. However, to our knowledge, the effect of collapsing supplement use into such categories has not been previously evaluated, and the relative validity of the resulting intake estimates is unknown and possibly unacceptable for many studies.

Participants in the Hawaii-Los Angeles Multiethnic Cohort Study provided detailed information on the type and brand of multivitamin supplement products that they consumed. We used these data to calculate daily nutrient intakes from multivitamin supplements. We then recalculated intakes assuming either single or multiple default values for the nutrient composition of the products and evaluated the impact of these assumptions on nutrient intake estimates.

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MATERIALS AND METHODS

Multiethnic cohort study. The Hawaii-Los Angeles Multiethnic Cohort Study was established to examine the relation of diet and other risk factors with cancer. The appropriate institutional review boards (University of Hawaii and University of Southern California) approved the study proposal. Baseline data were collected from 1993 to 1996, using a mailed questionnaire. The cohort consists of ~215,000 adults 45–75 y of age in 1993, largely from 5 principal racial/ethnic groups (African American, Japanese American, Latinos, Native Hawaiian, and white). Details of the study design and implementation are described elsewhere (29).

In 1999–2001, a follow-up questionnaire that requested detailed information on multivitamin supplement use was sent to all participants. The current analysis is based on participants in Hawaii who returned this questionnaire and who self-identified as belonging to one of the following racial/ethnic groups: Japanese Americans, Native Hawaiians, whites, or other Asians (Chinese, Filipinos, and Koreans). Of 103,899 participants from Hawaii, 84,575 (81%) met these criteria.

Nutrient intakes from supplements. The questionnaire asked participants if a multivitamin with or without minerals was used at least once a week during the previous year, and if so, to write in the specific brand and name of up to 3 products. Participants were also asked to indicate the average number of times the products were taken during the last year by choosing 1 of 5 frequencies: 1–3 times/wk, 4–6/wk, 1/d, 2/d, and >3/d. To estimate daily intakes, we divided weekly frequencies by 7 (e.g., 1–3 times/wk was converted to 2/7 or 0.3 of a dose/d). We assumed that participants took the dosage recommended on the product label, based on results from a previous calibration study that collected more detailed data on supplement use (20,30). For the majority of supplements, the recommended dose is 1 pill, but for a few supplements the recommendation is to take multiple pills or tablets. To calculate the actual daily nutrient intake from supplements, the daily frequency of use was multiplied by the nutrient composition per dose from the Supplement Composition Table (SCT) for each supplement product. The SCT has been compiled and maintained by the Cancer Research Center of Hawaii for use in the Multiethnic Cohort Study (20). Total nutrient intake from multivitamins was then calculated for each of 15 nutrients as the sum of up to 3 supplements reported.

For this study, a multivitamin supplement was defined as a product containing 2 or more vitamins, with or without minerals. Although 43,564 participants reported using multivitamin supplements, only 28,358 (65%) provided complete information on supplement manufacturer, brand name, product name, and frequency of use. The remaining 35% of multivitamin users gave insufficient information (e.g., manufacturer or brand name but without the name of the product) and the product could not be matched to our SCT. Therefore, these subjects were not included in our analyses. Frequency of use was omitted by <1% of supplement users. To exclude outliers, maximum acceptable levels of 15 nutrients were determined in a previous study (20) and were slightly modified for use here. Subjects who exceeded the maximum level for any of the nutrients were excluded from the study, resulting in a final sample of 26,735.

Assignment of supplements to categories. The estimated nutrient intake from multivitamins was also calculated after assigning each multivitamin supplement to broad categories and determining a default nutrient profile type. Products were categorized into 4 subtypes: one-a-day with minerals, one-a-day without minerals, B-complex or stress multivitamin, and antioxidant combination. The classification was primarily based on the name of the product. If the name of the product did not indicate 1 of the 4 subtypes, the profile of nutrients in the product was considered. A product containing ≥2 B vitamins with or without vitamin C or vitamin E, but with no other vitamin or mineral, was classified as a B-complex or stress multivitamin. The antioxidant combination type included products containing a combination of vitamin A, β-carotene, vitamin E, vitamin C, and selenium, but low levels of other vitamins or minerals. Multivitamin products that could not be classified by product name, and did not belong to 1 of 2 nutrient profiles above, were classified as one-a-day with or without minerals.

Calculation of default nutrient composition profiles. Two types of default nutrient profiles for a dose were determined: a single default profile for all multivitamins and 4 default profiles, 1 for each of the 4 subtypes of multivitamin supplements. Default values were calculated separately for each of 15 nutrients. The top and bottom 10% of multivitamin users were excluded from this calculation to reduce the effect of outliers on the default values. The default value for each nutrient was then computed as the value that minimized the sum of the squared deviations between the actual and estimated intakes across the middle 80% of the distribution for each nutrient. That is, the default value is the φ that minimizes the equation $\sum_{i=1}^{n}(\sum_{j=1}^{m} \omega_j f_{ij} - \sum_{j=1}^{m} \varphi f_{ij})^2$, where ω_j is the nutrient value per dose of supplement j, f_{ij} is the frequency of intake for supplement j for individual i, m is the number of supplements taken by individual i, and n is the number of multivitamin users. The value can be solved as

$$\varphi = \frac{\sum_{i=1}^{n}\left(\sum_{j=1}^{m} f_{ij}\right)\sum_{j=1}^{m}\omega_j f_{ij}}{\sum_{i=1}^{n}\left(\sum_{j=1}^{m} f_{ij}\right)^2}.$$

For default amounts of nutrients within each of the supplement types, the sum is minimized over supplements in the subtype.

Defaults were also computed as a mean composition of products weighted by the number of users; i.e., as $\lambda = \sum_{k=1}^{p} g_k\, \omega_k / \sum_{j=1}^{p} g_k$, where g_k is the number of users of supplement k and p is the total number of supplements reported. The estimated intakes from these 2 approaches led to similar results. However, the estimate from the first approach described above has desirable statistical properties because it considers all information available on supplement use, including the frequency of use for each individual as well as the number of users of each multivitamin product. Therefore, this approach was used to create the nutrient defaults used in this study.

Statistical analyses. The median and the 10th and 90th percentiles of nutrient intakes from multivitamins were calculated using detailed supplement composition data from multivitamin users who provided complete information. Intakes were then recalculated using 2 types of default values: *1*) a single default for all multivitamins and *2*) defaults for 4 categories of multivitamins. Finally, using the defaults, original (or "actual") intakes were compared with estimated intakes. The median nutrient levels and the 10th and 90th percentiles were also calculated for the nutrient composition of products that were reported.

The Wilcoxon Signed Rank test was used to test differences between actual intakes and estimated intakes, using either single or multiple defaults. Differences were considered significant when $P < 0.05$. Nutrient intakes from supplements were not normally distributed. Therefore, Spearman correlation coefficients were calculated to assess the relative agreement between default-based intakes and actual nutrient intakes from multivitamins. Data analysis was performed using SAS software, version 9.1 (SAS Institute).

RESULTS

Of the 26,735 multivitamin supplement users that provided complete information, 1656 (6.2%) reported using more than 1 product. The one-a-day type multivitamin with minerals was the most common product (reported by 91.6% of users) (**Table 1**). The B-complex or stress type and antioxidant combination type were reported by 4.3 and 3.1% of users, respectively. The total number of multivitamin supplement products reported by participants was 1246, of which 65.9% were classified as one-a-day type with minerals, 16.1% as B-complex or stress type, and 13.7% as antioxidant combination type. The proportions of subjects using each of the 4 subtypes were similar across ethnic and sex groups. The majority of reported multivitamins (77.7%) were taken 1/d, 6.7% were taken ≥2/d, and 15.6% of supplements were taken <1/d (1–6 times/wk).

The medians for the actual daily nutrient intakes from multivitamin supplements were identical in men and women

TABLE 1

Numbers of respondents and types of multivitamin supplements reported, Hawaii component of the Multiethnic Cohort Study, 1999–2001

	Hawaiian		Japanese American		White		Other Asian		
	Men	Women	Men	Women	Men	Women	Men	Women	Total
Participants, *n*	4784	6541	17673	20877	14315	14630	2079	3676	84575
Multivitamin users, *n*	1589	2747	7982	11848	7629	9196	715	1858	43564
Participants in the analyses,[1] *n*	893	1582	5018	7568	4631	5458	451	1134	26735
Participants using each type,[2]%									
One-a-day type with minerals	91.7	92.2	90.9	92.6	91.4	90.8	92.2	91.1	91.6
One-a-day type without minerals	2.6	2.5	3.7	3.3	3.5	3.8	4.0	2.9	3.3
B-complex or stress type	3.8	4.6	4.4	3.4	4.5	5.7	3.1	4.7	4.3
Antioxidant combination type	4.4	2.7	2.9	2.8	3.1	4.3	2.4	2.7	3.1
Products, *n*	221	309	492	585	624	700	116	223	1246
Products in each type, %									
One-a-day type with minerals	70.6	71.5	68.5	72.0	67.3	69.0	69.8	70.4	65.9
One-a-day type without minerals	6.8	5.5	4.3	4.3	5.3	5.4	12.9	5.4	4.3
B-complex or stress type	10.0	13.3	15.9	13.7	14.7	15.4	9.5	15.2	16.1
Antioxidant combination type	12.7	9.7	11.4	10.1	12.7	10.1	7.8	9.0	13.7

1 Only supplement users who provided a known product name are included in the analyses.
2 Percents do not sum to 100 because participants were asked to record up to 3 product names.

except for vitamin A (**Table 2**). Median vitamin intakes were well above the recommended daily value based on the recommended dietary allowances (RDAs) or the adequate intakes (AIs) (31–34) except for vitamin C and vitamin D; median vitamin B-12 intakes (25.0 μg/d in men and women) were >10 times the RDA (2.4 μg/d for both men and women). Median mineral intakes from multivitamin supplements were lower than the RDAs or the AIs, except for zinc. Intakes of nutrients from supplements were highly variable, with wide ranges between the 10th and 90th percentiles for both men and women for most nutrients. No large differences existed in nutrient intakes from supplements across the 4 ethnic groups (data not shown).

The nutrient composition of the products reported by supplement users also tended to be highly variable (**Table 3**). More than half of the products contained no β-carotene. The value of 90th percentile was 10 times higher than the median for thiamin, riboflavin, vitamin B-6, and iron. However, values for the median and 90th percentile were the same for folate and vitamin D, indicating that many products contained the same amount. The nutrient profile of the single default is similar to the default for the one-a-day type with minerals (Table 3), because this subtype was the product reported by the majority of participants. The levels of vitamins in the default for the one-a-day type without minerals were mostly lower than in the one-a-day type with minerals. The levels of thiamin and riboflavin

TABLE 2

Daily nutrient intake from multivitamin supplements among users, Hawaii component of the Multiethnic Cohort Study, 1999–2001[1]

			RDA or AI[2]	
Nutrient	Men, *n* = 10,993	Women, *n* = 15742	Men	Women
Vitamin A, RE,[3] μg	1100 (429, 2500)	1071 (500, 2400)	900 μg RAE[4]	700 μg RAE
β-carotene, μg	1071 (0, 3000)	1071 (0, 2571)	—	—
Thiamin, *mg*	1.5 (1.1, 20.0)	1.5 (1.1, 15.0)	1.2	1.1
Riboflavin, *mg*	1.7 (1.2, 20.0)	1.7 (1.2, 15.7)	1.3	1.1
Niacin, *mg*	20.0 (11.7, 50.0)	20.0 (11.7, 50.0)	16	14
Vitamin B-6, *mg*	3.0 (1.4, 21.0)	3.0 (1.4, 17.9)	1.7	1.5
Vitamin B-12, μg	25.0 (6.0, 31.0)	25.0 (6.0, 30.0)	2.4	2.4
Folate, DFE,[5] μg	680 (194, 680)	680 (194, 680)	400	400
Vitamin C, *mg*	60.0 (42.9, 330)	60.0 (42.9, 250)	90	75
Vitamin D,[6] *IU*	400 (114, 400)	400 (114, 400)	400/600[7]	400/600
Vitamin E,[8] α-TE, *mg*	20.3 (6.8, 51.4)	20.3 (6.8, 45.0)	15 mg α-tocopherol	15 mg α-tocopherol
Calcium, *mg*	200 (0, 300)	200 (0, 429)	1200	1200
Iron, *mg*	4.0 (0, 18.0)	4.0 (0, 18.0)	8	8
Zinc, *mg*	15.0 (4.3, 22.5)	15.0 (4.3, 22.5)	11	8
Selenium, μg	20.0 (0, 100)	20.0 (0, 70.0)	55	55

1 Values are medians (10th percentile, 90th percentile).
2 RDA, recommended dietary allowance for >50 y of age; AI, adequate intake for >50 y of age (31–34).
3 RE, retinol equivalent.
4 RAE, retinol activity equivalent.
5 DFE, dietary folate equivalent.
6 1 IU of vitamin D = 0.025 μg of calciferol.
7 51–70 y/>70 y.
8 α-TE, α-tocopherol equivalent.

TABLE 3

Composition of multivitamin products and default values per dose used to estimate nutrient intakes from supplements, Hawaii component of the Multiethnic Cohort Study, 1999–2001

			Defaults by subtype[2]			
Nutrient	Composition[1]	Single default[2]	One-a-day with minerals	One-a-day without minerals	B-complex or stress	Antioxidant combination
Vitamin A, RE,[3] *μg*	1375 (0, 3000)	1086	1211	1287	0	664
β-carotene, *μg*	0 (0, 6000)	748	909	272	0	243
Thiamin, *mg*	5.0 (0, 50.0)	2.4	2.5	1.9	7.0	0.1
Riboflavin, *mg*	5.1 (0, 50.0)	2.6	2.6	2.1	7.2	0.7
Niacin, *mg*	20.0 (0, 100)	18.6	20.5	19.6	19.3	7.0
Vitamin B-6, *mg*	5.0 (0, 50.0)	3.2	3.4	2.6	4.9	1.1
Vitamin B-12, *μg*	12.0 (0, 100)	14.8	17.5	6.7	9.8	1.2
Folate, DFE,[4] *μg*	680 (0, 680)	527	589	674	473	27.0
Vitamin C, *mg*	120 (0, 600)	75.6	80.2	72.3	86.2	100
Vitamin D, *IU*[5]	400 (0, 400)	340	366	382	0	8.4
Vitamin E, α-TE,[6] *mg*	20.3 (0, 180)	16.6	18.5	13.5	9.6	16.5
Calcium, *mg*	54.3 (0, 498)	198	172	0	9.3	27.2
Iron, *mg*	1.7 (0, 18.0)	6.6	7.6	0	2.6	0.0
Zinc, *mg*	15.0 (0, 22.6)	12.8	14.2	0	4.4	5.9
Selenium, *μg*	20.0 (0, 100)	19.7	21.9	0	5.0	24.5

1 Values are medians (10th percentile, 90th percentile), $n = 1246$.
2 Default values were calculated to minimize the sum of the squared deviations, $\sum$ (actual intake – estimated intake)^2. Actual intake = the nutrient value per dose from SCT × daily frequency, summed across supplements for each individual. Estimated intake = the default nutrient value per dose × daily frequency, summed across supplements for each individual.
3 RE, retinol equivalents.
4 DFE, dietary folate equivalents.
5 One IU of vitamin D = 0.025 μg of calciferol.
6 α-TE, α-tocopherol equivalents.

for the B-complex or stress default were much higher than for the one-a-day types. For the antioxidant combination default, the vitamin C level was higher than for the other subtypes, levels of vitamin E and selenium were similar to the one-a-day with minerals, and the vitamin A level was lower.

The median daily nutrient intake, calculated using multiple defaults, tended to be higher than the median intake using only a single default (**Table 4**). However, the validity of the default values, relative to the actual median intake, varied across nutrients. For β-carotene, niacin, vitamin B-12, folate, vitamin

TABLE 4

Comparison of estimated daily nutrient intake using default values and actual intakes from multivitamin supplements, Hawaii component of the Multiethnic Cohort Study, 1999–2001[1]

	Estimated intake		
Nutrient	Single default	Multiple defaults	Actual intake[2]
Vitamin A, RE,[3] *μg*	1086 (776, 1551)	1211 (346, 1287)	1071 (450, 2500)
β-carotene, *μg*	748 (534, 1068)	909 (260, 909)	1071 (0, 2970)
Thiamin, *mg*	2.4 (1.7, 3.4)	2.5 (1.7, 3.5)	1.5 (1.1, 15.0)
Riboflavin, *mg*	2.6 (1.8, 3.6)	2.6 (1.9, 4.1)	1.7 (1.2, 17.0)
Niacin, *mg*	18.6 (13.3, 26.6)	20.5 (14.0, 20.5)	20.0 (11.7, 50.0)
Vitamin B-6, *mg*	3.2 (2.3, 4.6)	3.4 (2.4, 4.5)	3.0 (1.4, 20.0)
Vitamin B-12, *μg*	14.8 (10.6, 21.2)	17.5 (6.7, 17.5)	25.0 (6.0, 30.0)
Folate, DFE,[4] *μg*	527 (376, 752)	589 (338, 674)	680 (194, 680)
Vitamin C, *mg*	75.6 (54.0, 108)	80.2 (57.3, 86.2)	60.0 (42.9, 300)
Vitamin D, *IU*[5]	340 (243, 486)	366 (104, 366)	400 (114, 400)
Vitamin E, α-TE,[6] *mg*	16.6 (11.9, 23.7)	18.5 (9.6, 18.5)	20.3 (6.8, 45)
Calcium, *mg*	198 (142, 283)	172 (49.0, 171.5)	200 (0, 385)
Iron, *mg*	6.6 (4.7, 9.4)	7.6 (2.2, 7.6)	4.0 (0, 18.0)
Zinc, *mg*	12.8 (9.1, 18.3)	14.2 (4.114.2)	15.0 (4.3, 22.5)
Selenium, *μg*	19.7 (14.1, 28.2)	21.9 (6.3, 21.9)	20.0 (0, 87.5)

1 Values are medians (10th percentile, 90th percentile), $n = 26{,}735$.
2 Wilcoxon Signed Rank Test comparing estimated intake, using either single default or multiple defaults to actual intakes, were all significant at $P < 0.001$.
3 RE, retinol equivalents.
4 DFE, dietary folate equivalents.
5 One IU of vitamin D = 0.025 μg of calciferol.
6 α-TE, α-tocopherol equivalents.

D, vitamin E, and zinc, using multiple defaults worked well for estimating actual median intake, whereas for vitamin A, vitamin B-6, vitamin C, calcium, iron, and selenium, using a single default was closer to the actual median intake. However, the differences between actual and estimated intakes, using either single or multiple defaults, were significant for all nutrients ($P < 0.05$).

For all nutrients except niacin, Spearman correlations between intakes calculated from defaults and actual intakes were higher using multiple defaults than using a single default (**Table 5**). In general, correlations using multiple defaults were >0.5 ($P < 0.001$), although they were lower for β-carotene (0.29, $P < 0.001$), vitamin B-12 (0.44, $P < 0.001$) and iron (0.45, $P < 0.001$). The correlations between the actual intake and intake assuming a single default were lower, with only 5 values >0.5. We also examined the effect of using ethnic or sex specific defaults, rather than overall defaults, and found very similar correlations to those in Table 5 (data not shown).

DISCUSSION

Median daily nutrient intakes from multivitamins among supplement users were high, usually above the RDAs or AIs for nutrients examined in this study. Nutrient intakes from multivitamins were also highly variable among individuals, with a wide range between the 10th and 90th percentiles. Over 1200 different brands of multivitamins were reported by participants. Although most multivitamin users reported using products from the one-a-day with mineral subtype, there was substantial variability in the composition of nutrients in multivitamins across subtypes, and even within the same subtype. This variation in composition can lead to significant differences in nutrient intakes from supplements among users. Differences in the frequency of multivitamin use did not contribute importantly to the variation in nutrient intake, because the majority of multivitamins (77.7%) were taken once a day. The nutrient intake of multivitamin users could be ranked relatively accurately with 4 default nutrient profiles, but correlations were lower with the single-default profile.

TABLE 5

Spearman correlation coefficients between estimated daily intake using defaults and actual intake from multivitamin supplements, Hawaii component of the Multiethnic Cohort Study, 1999–2001[1]

Nutrient	Single default	Multiple defaults
Vitamin A	0.47	0.59
β-carotene	0.24	0.29
Thiamin	0.49	0.61
Riboflavin	0.49	0.58
Niacin	0.61	0.61
Vitamin B-6	0.48	0.59
Vitamin B-12	0.33	0.44
Folate	0.58	0.68
Vitamin C	0.54	0.55
Vitamin D	0.57	0.80
Vitamin E	0.47	0.55
Calcium	0.39	0.64
Iron	0.23	0.45
Zinc	0.52	0.68
Selenium	0.34	0.50

1 For supplement users who provided complete information, and includes those who reported multiple supplements, ($n = 26{,}735$). All correlation coefficients are significant at $P < 0.001$.

Other studies also have found high intakes from multivitamins (19,21,35,36), including previous publications on intakes among the Multiethnic Cohort Study participants (20,24). These findings emphasize the importance of carefully evaluating alternative methods of collecting and quantifying supplement use from multivitamins.

We did not find published studies that examined the effect of collapsing detailed information on supplement use into broad categories. Patterson et al. (19) examined the effect of imputing 1 value for each of 3 nutrients in multivitamins, and found good Spearman correlations with actual intake levels for vitamin E (0.84) and folic acid (0.61), and a poor correlation for iron (0.29). The correlations in our study were 0.55 for vitamin E, 0.68 for folic acid, and 0.45 for iron. Patterson et al. (19) imputed nutrients for only 3 subtypes of supplements (one-a-day type without minerals, one-a-day type with minerals, and stress supplements) and used the exact nutrient composition for all other mixtures and single supplements. Thus, their study is not strictly comparable to ours. Patterson et al. have also reported that inaccurate assumptions about the micronutrient composition of multiple vitamins were a major source of error in estimating nutrient intakes from supplements (18).

We found substantial variation in the nutrient composition of the multivitamin products within each subtype. For example, some of the products classified into the one-a-day type had a very different nutrient composition compared with leading brands reported by the majority of participants. It is possible that more refined classification schemes for multivitamin subtypes could further minimize the variance within subtype. Also, the classification of supplements was done by the investigators and may not correspond to participant perception of supplement groupings. If these subtypes are used on a questionnaire, participants may have difficulty knowing which products belong in each subtype. Therefore, if survey instruments provide several questions asking about subtypes of multivitamin supplements, detailed instructions should be given so that participants can choose the appropriate subtype. For instance, in the current study, 1360 (1.6%) of 84,575 participants reported supplements taken for bone health as multivitamin supplements, even though most of these products do not contain more than 1 vitamin (usually, only vitamin D plus minerals, such as calcium). To capture information on nutrient intakes from bone-related products, it would be less confusing if questionnaires had a specific category under single supplements so that participants do not mistakenly report them as multivitamins.

The questionnaire used for this study was open-ended and thus captured information on multivitamin supplements in detail. Product names and supplement composition, as well as frequency of use during the last year, were used to calculate nutrient intakes. Although this method was considered a "gold standard" measure of usual multivitamin supplement intake for the study, these intakes are probably not completely accurate for several reasons: the frequency and dose may have been reported inaccurately, subjects may not have included all of the multivitamins that they took, and usage may have varied over the year covered by the questionnaire.

When calculating defaults, we were able to use the data for only 65% of supplement users because the other 35% did not report enough details to precisely identify the supplement used. It is possible that the defaults would have been different if it were possible to reestablish contact with these participants for more details. However, incomplete information provided by participants is a common problem that prevents investigators from assessing the exposures accurately in large studies, which is why it is important to develop appropriate default values.

The Hawaii component of the Multiethnic Cohort Study contains large numbers of participants from each of 4 ethnic groups in one specific region of the U.S. (Hawaii). Therefore, the defaults may not apply to other ethnic groups or to other regions. However, we did not find that ethnic-specific default values improved the accuracy of intake estimates in our study.

Because it is seldom possible to collect detailed information on the exact brand of multivitamins used, large surveys often ask only about the use of supplement types. To quantify nutrient intake, a default composition must be assumed, which can be a more complex process for multivitamins than for single vitamin or mineral supplements. Understanding the types of errors introduced by these defaults is crucial. As shown in this analysis, the use of multiple subtype categories, with default nutrient profiles for each, gives better correlations with actual nutrient intakes than a single question and default profile. Thus, well-defined multiple-default values can rank nutrient intakes more correctly within the study population. Additionally, the relation between nutrient intakes, from foods plus supplements, and disease outcomes will more likely reflect true associations if the level of measurement error is reduced. Furthermore, people at risk of extreme intakes for certain nutrients due to overuse of supplements can be identified. To derive appropriate default compositions to be assigned to the multivitamin subtypes in a particular population, a substudy should be conducted to collect the product names for a representative subsample.

In conclusion, we found that a substantial portion of the Multiethnic Cohort Study participants used multivitamin supplements, that the composition of these supplements was highly variable, and that the supplements contributed substantially to the intakes of nutrients. To estimate nutrient intakes from dietary supplements most accurately, brand and product information should be collected so as to identify the exact supplement composition. However, when collecting such detailed information is not practical, our findings suggest that asking questions about the type of multivitamin product substantially improves the accuracy of nutrient intake estimates, compared with a single question about multivitamin use.

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